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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/661,784      | 09/15/2003  | Fernando Donate      | 38342-193024        | 7260             |

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EXAMINER

DESAI, ANAND U

ART UNIT PAPER NUMBER

1653

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                   |                               |  |
|------------------------------|-----------------------------------|-------------------------------|--|
| <b>Office Action Summary</b> | Application No.<br>10/661,784     | Applicant(s)<br>DONATE ET AL. |  |
|                              | Examiner<br>Anand U. Desai, Ph.D. | Art Unit<br>1653              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 14-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>20041103</u> . | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

1. This office action is in response to Amendment filed on April 28, 2005. Claims 14-42 were previously withdrawn as being drawn to nonelected inventions. Claims 1-13 are currently pending and are under examination.

#### ***Information Disclosure Statement***

2. The information disclosure statement (IDS) submitted on November 3, 2004 is being considered by the examiner.

#### **Withdrawal of Rejections**

3. The rejection of claims 3-7, and 10-13 under 35 U.S.C. 112, second paragraph as being indefinite is withdrawn based on Applicants' amendment to the claims.

4. The rejection of claims 1-3, 8-10, and 13 under 35 U.S.C. 102(b) as being anticipated by McCrae, R. (WO 00/35407) is withdrawn based on Applicants' amendment to the claims.

5. The rejection of claims 1, and 2 under 35 U.S.C. 102(a) as being anticipated by Zhang et al. (Can. J. Physiol. Pharmacol. 80: 85-90 (2002)) is withdrawn based on Applicants' amendment to the claims.

6. The rejection of claims 1-13 under 35 U.S.C. 103(a) as being obvious over McCrae, R. (WO 00/35407) in view of Piwnica-Worms (U.S. Patent 6,348,185 B1) is withdrawn based on Applicants' amendment to the claims.

7. The rejection of claims 1-13 under 35 U.S.C. 103(a) as being obvious over Zhang et al. (Can. J. Physiol. Pharmacol. 80: 85-90 (2002)) in view of Piwnica-Worms (U.S. Patent 6,348,185 B1) is withdrawn based on Applicants' amendment to the claims.

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## Maintenance of Objections and Rejections

### *Specification*

8. The disclosure is objected to because of the following informalities: The amendment submitted on April 28, 2005, identifies paragraph [0051] twice. It appears as though the second presentation of [0051] should be [0052]; Paragraph [0052] is being amended.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The added material that is not supported by the original disclosure, is a variant of native HK-D3 (SEQ ID NO: 1), which is a substitution variant wherein a seven residue C-terminal sequence is replaced **without** the addition of two amino acids to the amino-terminus. The specification does disclose at paragraphs [0051-0052] variants that are encompassed by an addition of two amino acids at the amino-terminus **and** including a substitution variant wherein a seven residue C-terminal sequence is replaced. Applicant is required to cancel the new matter in the reply to this Office Action. Suggest removing the word,

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“or” in Claim 1(c), “...addition variant of two amino acids and ~~and/or~~ a substitution variant wherein...”

11. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a variant of an anti-angiogenic polypeptide having the sequence identified as either SEQ ID NO: 1 or 3. To satisfy the written description requirement, the specification must describe the invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. The specification does not describe the structure, that is amino acids in the various polypeptides that can be altered without affecting the function of a specific polypeptide. For one to be in possession of the claimed invention, the inventor would have to know the functional consequences of structural alterations. Thus due to the limited predictability in the art, a skilled artisan would not find adequate support for variants of an anti-angiogenic polypeptide as disclosed in claim 1 in the specification. Claims 2-13 are rejected for depending on a rejected base claim.

#### Response to Remarks

12. Applicants believe the specification does provide adequate written description for the claims as filed. Applicants believe the Office is underestimating the relative facility in the art today to predict effects of amino acid substitutions, and to screen the substitutions in the

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appropriate biological assays. Applicants state that it is almost trivial to predict and then test which variants fall inside or outside the scope of the functional limitations of claim 1.

Applicants believe the amended claim 1 drawn to conservative substitution variants and variants with amino-terminal additions and carboxy-terminal replacements would comply with the written description requirement of 35 U.S.C. § 112.

Applicant's arguments filed April 28, 2005 have been fully considered but they are not persuasive. Due to the limited predictability in the art, a skilled artisan would not find adequate support for the variants currently claimed. Isordia-Salas, I. et al. disclose a Ser<sup>511</sup> to Asn<sup>511</sup> variant of high molecular weight kininogen in Lewis rats that produces a change in the rate of formation of cleavage product, bradykinin, which might be a contributing factor to chronic inflammation in Lewis rats (see Abstract, and page 2838, Results, Single point mutation in Lewis HK gene that distinguishes it from Buffalo and Fischer HK genes, 1<sup>st</sup> paragraph, last sentence, Figure 2A and B). Isordia-Salas, I. et al. also cite Picard, V. et al. to disclose a Thr to Ser conservative substitution variant, that results in the addition of protein function for an isoform of antithrombin III with enhanced heparin affinity (see page 2841, Discussion, Right hand column, 2<sup>nd</sup> paragraph). Therefore, the art has shown that a conservative amino acid substitution in a protein, results in unpredictable functional effects. Thus, a skilled artisan would not find adequate support for variants, conservative or non-conservative, of an anti-angiogenic polypeptide as disclosed in claim 1.

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Art of Record

13. McCrae, K. (U.S. Patent 6,869,931 B1) claims priority to U.S. Provisional application 60/112,427, which is the same priority document for WO 00/35407 currently being cited in the 35 U.S.C. 103 rejection. The disclosures appear to be duplicates.

*Conclusion*

14. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

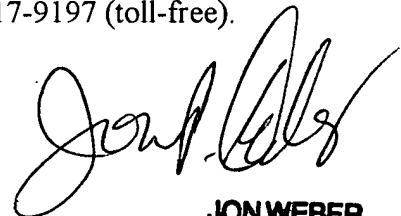
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 7:00 a.m. - 3:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 21, 2005



**JON WEBER**  
**SUPERVISORY PATENT EXAMINER**